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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/629,975	07/30/2003	James Hunter Boone	TLAB.79219	9513

5251 7590 09/20/2005

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EXAMINER	
COOK, LISA V	

ART UNIT	PAPER NUMBER
1641	

DATE MAILED: 09/20/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action Before the Filing of an Appeal Brief	Application No. 10/629,975	Applicant(s) BOONE ET AL.	
	Examiner Lisa V. Cook	Art Unit 1641	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 15 August 2005 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☒ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:
   a) ☐ The period for reply expires _____months from the mailing date of the final rejection.
   b) ☒ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

   Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☐ The Notice of Appeal was filed on _____. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☒ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
   (a) ☒ They raise new issues that would require further consideration and/or search (see NOTE below);
   (b) ☐ They raise the issue of new matter (see NOTE below);
   (c) ☒ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
   (d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: *See Continuation Sheet*. (See 37 CFR 1.116 and 41.33(a)).
4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5. ☒ Applicant's reply has overcome the following rejection(s): under 112, 2nd.
6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7. ☒ For purposes of appeal, the proposed amendment(s): a) ☒ will not be entered, or b) ☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
   The status of the claim(s) is (or will be) as follows:
   Claim(s) allowed: *NONE*.
   Claim(s) objected to: *NONE*.
   Claim(s) rejected: *1-6*.
   Claim(s) withdrawn from consideration: *NONE*.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: See attached.
12. ☐ Note the attached Information Disclosure Statement(s). (PTO/SB/08 or PTO-1449) Paper No(s). _____
13. ☐ Other: _____.

Lisa V. Cook
8/8/05

LONG V. LE
SUPERVISORY PATENT EXAMINER
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Continuation of 3. NOTE: the amendment introduces new claim limitations that require additional search and considerationof the prior art. For example linear curve determinations. Please note the claims are viewed in light of the specification, however limitations from the specification are not read into the claims.

ADVISORY ACTION

Request for Reconsideration

1. Applicants response to the Final Office Action mailed June 14, 2005 is acknowledged (paper filed August 15, 2005). The amendment filed on August 15, 2005 will not be entered because it raises new issues (See form PTOL-303 attached). Currently, claims 1-6 are pending and currently under consideration.

OBJECTIONS WITHDRAWN

Information Disclosure Statement

2. The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609 A(1) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the examiner on form PTO-892 or applicant on PTO-1449 has cited the references they have not been considered.

Response to Arguments

Applicant contends that all references cited in the specification were properly submitted by way of an Information Disclosure Statement in parent application US Serial No.10/002,842. The IDS in parent application US Serial No.10/002,842 has been considered. It is not necessary for Applicant to submit a separate IDS in the present application. See MPEP 609. The objection is withdrawn.

REJECTIONS WITHDRAWN

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

3. Claims 1 and 2 are withdrawn from rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. Claim 1 is vague and indefinite in reciting "total" endogenous lactoferrin because it is not clear as to what the term "total" encompasses. As recited the metes and bounds of the claim cannot be determined. The term "total" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. Is it applicant's intent to mean that all the lactoferrin (whole and half-sized) found in the sample will be detected? Please clarify.

Applicant contends that "total" is intended to describe whole and smaller degraded lactoferrin, which is able to bind polyclonal antibodies. This argument was carefully considered and found persuasive. Accordingly the rejection is withdrawn.

B. The term "within a linear portion" in claim 2 is a relative term which renders the claim indefinite. It is not clear as to what applicant considers a linear portion of the standard curve. Will any measurement on the standard curve meet the instantly claimed limitation? The term "within a linear portion" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. In order to obviate this rejection it is suggested that "within a linear portion" be removed from the claim.

Applicant contends that the specification(section 0059) describes the preparation of the standard curve as well as the determination of the linear portion of the curve. This argument was carefully considered and found persuasive. The rejection is withdrawn.

REJECTIONS MAINTAINED

Claim Rejections - 35 USC § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

I. Claim 6 is rejected under 35 U.S.C. 102(b) as being anticipated by Sugi et al. (The American Journal of Gastroenterology, Vol.91, No.5, 927-934, 1996).

Sugi et al. disclose that lactoferrin (LF) levels were elevated in fecal samples of patients with inflammatory bowel disease. See abstract. The ELISA assay procedure is disclosed on page 928. LF elevation was seen in various disease states. Sugi et al. measure multiple samples at different times (1st and 2nd samples wherein the second sample concentration is measured at a time later than the first sample measurement). In particular the multiple sampling analysis is seen on page 929 in figure 2 for example. LF concentrations are measured at different time intervals, which include 24hours, 48hours, 72hours, and 96hours. The LF concentrations are subsequently compared to each other in figure 2 – A, B, and C (48hrs – 72hours –96 hours are all later than the first 24hour LF detection).

Response to Arguments

Applicant contends that Sugi et al. do not describe each and every element set forth in the rejected claims.

Specifically applicant argues that Sugi et al. teach a method of reading the same fecal sample at a first time and a second time, while the instant method detects different samples at a first and second time. This argument was carefully considered but not found persuasive because

Sugi et al. teach samples collected from the same patient (UC and CD) at two or more times (see page 928 2nd column 1st paragraph). The samples were also collection from different samples (from various patients) at times varying from 48 to 72 hours (the samples are not all the same). See page 928 1st column last paragraph –Subjects to 2nd column 2nd paragraph – Method of stool collection. The samples are collected independently but are compared to each other in order to evaluate differences there between in figure 3 for example.

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

II. Claims 1-3 are rejected under 35 U.S.C.103(a) as being unpatentable over Uchida et al. (US Patent #5,552,292).

Uchida et al. teach methods to measure lactoferrin in fecal samples. Lactoferrin is taught to be a marker for various diseases related to inflammatory gastrointestinal disorders and colon cancer. Column 2 lines 46-59.

Lactoferrin was found to be the most stable substance in feces. Column 3 lines 10-11. Specifically a polyclonal antibody for lactoferrin (DAKOPATT) is employed to measure lactoferrin in inflammatory diarrhea specimens. Column 5 lines 57-61.

The method was performed in an enzyme-linked immunoassay format. A polyclonal antibody against lactoferrin (anti-human lactoferrin antibody) is immobilized onto wells of a 96-well polystyrene micro plate. The plate is contacted with diluted fecal specimen (column 11 lines 31-33 wherein 50Tl of sample is added to 100Tl %1BSA and TBS buffer) and detected with a polyclonal antibody labeled with alkaline phosphatase (anti-human-lactoferrin antibody). See column 11 example 2 and column 5 lines 14-19. The results were correlated to standards prepared with purified lactoferrin. Column 6 lines 13-19.

The assay results were detected at 510/630nm absorbance. Column 11 lines 53-56. Increased levels of lactoferrin were demonstrated to several diseases. See column 12-Results.

Uchida et al. disclose standard curve comparative analyses (claim 2). Healthy person fecal samples were run and graphed on a curve for comparison to unknown sample sets (standard curve). Column 7 lines 51-64 and column 8 lines 18-29.

Kit embodiments are also disclosed. The kit contains antibodies immobilized on a solid phase (micro plate), an enzyme linked antibody, and a chromogene (enzyme substrate for color development). See column 4 lines 1-9 and column 5 lines 36-40.

With respect to endogenous lactoferrin, it is noted that the lactoferrin detected by Uchida et al. were found within the patient (endogenous to the patient) and occurred as a result of disorders.

Normal patients exhibited very small amounts of lactoferrin (0.75 – 2.4Tg/g feces) and Uchida et al. taught that their method could be used in various types of lactoferrin (column 6 lines 58-61). Therefore absent evidence to the contrary Uchida et al. teach the detection of endogenous lactoferrin.

Uchida et al. differ fro the instant invention in not specifically teaching sample detection at 450nm. However, Uchida et al. teach that the absorbance measurement is routinely adjusted to optimize the assay. See column 5 lines 30-32. Absent evidence to the contrary the detection of the lactoferrin assay taught by Uchida et al. is routine optimization. It would have been obvious to one having ordinary skill in the art at the time of the invention was made to measure lactoferrin at a 450nm absorbance reading, since it has been held that discovering an optimal value of a result effective variable involves only routine skill in the art. In re Boesch, 617 F.2d 272, 205, USPQ 215(CCPA 1980).

III. Claims 4 and 5 are rejected under 35 U.S.C.103(a) as being unpatentable over Uchida et al. (US Patent #5,552,292) in view of Foster et al. (U.S. Patent#4,444,879).

Please see Uchida et al. as set forth above.

Although Uchida et al. teach the regents required by the claims, they do not specifically teach the inclusion of all the reagents in kit configurations (in particularly the purified human lactoferrin – taught in '292 column in column 6 lines 14-16 and stop solution or coloring reagent – taught in '292 column 5 line 29-30). In other words, the reference fails to teach all the reagents as a kit. However, kits are well known embodiments for assay reagents. Foster et al. (U.S. Patent #4,444,879) describe one example.

In their patent kits including the reactant reagents, a micro plate, positive controls, negative controls, standards, and instructions are taught. The reagents are compartmentalized or packaged separately for utility. See figure 6, and column 15, lines 10-34.

It would have been prima facie obvious to one of ordinary skill in the art at the time of applicant's invention to take the detection assay reagents as taught by Uchida et al. and format them into a kit because Foster et al. teach that it is convenient to do so and one can enhance sensitivity of a method by providing reagents as a kit. Further, the reagents in a kit are available in pre-measured amounts, which eliminates the variability that can occur when performing the assay. Kits are also economically beneficial in reagent distribution.

Response to Arguments

Applicant contends that the Uchida reference fails to teach or suggest all the limitations of the rejected claims.

Specifically applicant argues that Uchida measures the level of only whole-sized lactoferrin by immunoassay utilizing monoclonal antibodies. This argument was carefully considered but not found persuasive because Uchida discloses the detection of total lactoferrin (whole and half-sized) with a polyclonal antibody. Lactoferrin was measured by immunoassay utilizing polyclonal antibody (DAKOPATT, Denmark, referred to as DAKO). The results showed two types of lactoferrin; whole and half-sized. See column 5 lines 57 through column 6 line 2.

Further, the test for obviousness is not whether the features of one reference may be bodily incorporated into the other to produce the claimed subject matter but simply what the combination of references makes obvious to one of ordinary skill in the pertinent art. See, *In re Bent,* 52 CCPA 850, 144 USPQ.28 (1964); *In re Nievelt,* 179 USPQ 224 (CCPA 1973).

Applicant's arguments with respect to the measurement of lactoferrein against a standard curve have been considered but are not persuasive because Uchida teaches this limitation in column 11 line 64-66 for example.

Limitations introduced by the amendment filed 8/15/05 have not been considered because the amendment has not been entered.

Applicant contends that the rejections under 103(a) including Foster 4,444,879 should be withdrawn because of the deficiencies noted in Uchida et al. The deficiencies in Uchida et al. have been addressed above. Accordingly, the rejections are maintained.

7. For reasons aforementioned, no claims are allowed.

Remarks

8. Prior art made of record and not relied upon is considered pertinent to the applicant's disclosure:

A. Tabata et al. (Rinsho Byori, 1997, 45(12), 1201-1203 – Abstract Only) teach that lactoferrin is useful in monitoring inflammatory bowel disease.

B. Mathias et al. (Digestive Diseases and Sciences, June 1994, Vol.39, No.6, 1155-1162) disclose methods for assessing bowel disease detecting duplicate patient samples to allow for test drug assessment (leuprolide). See abstract and page 1160-Discussion.

9. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform to the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The Group 1641 – Central Fax number is (571) 273-8300, which is able to receive transmissions 24 hours/day, 7 days/week. In the event Applicant would like to fax an unofficial communication, the Examiner should be contacted for the appropriate Right Fax number.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lisa V. Cook whose telephone number is (571) 272-0816. The examiner can normally be reached on Monday - Friday from 7:00 AM - 4:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le, can be reached on (571) 272-0823.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group TC 1600 whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR.

Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see httpr//pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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